REMARKS

Claims 1, 130, 138-140, and 143-145 have been amended. New claims 151 and 152 have been added. Claims 1, 60, 61, 130, 133, 138-140, 143-145, 151 and 152 are pending in the instant application.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance.

I. Priority

The Office Action stated that the priority date for the instant invention is taken to be September 24, 2003, the filing date of the instant application on the ground that Provisional Application 60/413,057, filed September 24, 2002, fails to disclose chymotrypsin variants, wherein the positions corresponding to positions 144, 193, 198, 201, 218, 223, 227, 228, 229, 230, and 231 of SEQ ID NO: 2 have been substituted with all possible amino acid residues.

Applicants disclose on page 11, lines 18-23, of the specification of Provisional Application 60/413,057, that "the trypsin mutant with chymotrypsin-like activity comprises (i) the same and/or similar substitutions corresponding to one or more substitutions selected from the group consisting of V144T, S193A, D198S, Q201M, A218I, N223S, R227S, P228T, N229S, Y230T, and S231P of amino acids 25 to 248 of SEQ ID NO: 2, (ii) one or more deletions corresponding to V192, K197, and A226 of amino acids 25 to 248 of SEQ ID NO: 2, and (iii) an insertion of T between G224 and C225 of amino acids 25 to 248 of SEQ ID NO: 2." Applicant submits that the language above does disclose chymotrypsin variants, wherein the positions corresponding to positions 144, 193, 198, 201, 218, 223, 227, 228, 229, 230, and 231 of SEQ ID NO: 2 have been substituted with all possible amino acid residues.

II. Objection

The Office Action objected to Figure 3 for disclosing sequences that are not identified by a sequence identifier number and corrrection was requested.

Applicants have amended the legend for Figure 3 to recite: "Figure 3 shows a comparative alignment of the amino acid sequences of a *Fusarium oxysporum* trypsin (SEQ ID NO: 2), a *Fusarium oxysporum* trypsin mutant having chymotrypsin activity (SEQ ID NO: 4), and bovine chymotrypsin A (SEQ ID NO: 24)." Support for SEQ ID NO: 24 is found in Figure 3.

Applicants submit a new Sequence Listing to replace the current Sequence Listing. The new Sequence Listing contains SEQ ID NO: 24. The content of the new Sequence Listing

contains no new matter.

III. Specification

The Office Action objected to the specification on the ground that the legend to Figure 3 states that a gene is disclosed in said figure, but there are only proteins disclosed in Figure 3; no genes or polynucleotides are disclosed therein.

Applicants have amended the legend for Figure 3 as described in Section II above.

IV. The Rejection of Claims 1, 60, 61, 130, 133, 138-140, and 143-145 under 35 U.S.C. § 112, Second Paragraph

Claims 1, 60, 61, 130, 133, 138-140, and 143-145 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for recitation of the phrase "microbial trypsin". The Office Action stated:

> The specification fails to formally define the phrase "microbial trypsin". The skilled artisan would assume that said phrase encompasses only enzymes expressed by a microbial cell. Applicants' assertion that "microbial trypsin" also encompasses any variant of any naturally occurring enzyme renders the claims indefinite. For purposes of clarity, it is suggested that the phrase "microbial trypsin" on Claim 1, line 9, as well as Claims 138-140, and 143-145, line 1 for each, be amended to "trypsin polypeptide".

Applicants have amended the term "microbial trypsin" to read "trypsin polypeptide" according to the Office's suggestion.

For the foregoing reason, Applicants submit that the claims overcome the rejections under 35 U.S.C. § 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. The Rejection of Claims 1, 61, 130, 133, 138-140, and 143-145 under 35 U.S.C. § 112, First Paragraph

Claims 1, 61, 130, 133, 138-140, and 143-145 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Office Action stated:

> It is acknowledged that the claims have been amended such that the trypsin polypeptide has at least 90% homology to residues 25-248 of SEQ ID NO: 2 or is encoded by a polypeptide that hybridizes under medium-high stringency with residues 202-801 of SEQ ID NO: 1. Said amendment dramatically reduces the genus of trypsin polypeptides used as "parent" molecules for making the recited variants having chymotrypsin activity. The skilled artisan would be enabled for identifying said genus of trypsin polypeptides. Therefore, this basis of the rejection is withdrawn.

> It is acknowledged that the principle question under 35 USC 112 is whether undue experimentation is required to practice the invention. As per *In re Wands*, the factors used to answer said question includes the breath of the claims. The instant invention encompasses any variant polypeptide having any structure and having chymotrypsin activity. It is acknowledged that the genus of parent trypsin molecule is limited to those having at least 90% homology to residues 25-248 of SEQ ID NO: 2 or is encoded by a polypeptide that hybridizes under medium-high stringency with residues 202-801 of SEQ ID NO: 1. It is also acknowledged that the recited variants are derived from said parent trypsin polypeptide wherein, 12 specific positions analogous to SEQ ID NO: 2 have been substituted, 3 specific positions analogous to SEQ ID NO: 2 have been deleted, and there is any insertion between the two positions analogous to 224 and 225 of SEQ ID NO: 2. However, these structural limitations describe the parent polypeptide; the claims fail to provide any structural limitation for the recited genus of variant polypeptides having chymotrypsin activity. It is acknowledged that Applicants' invention is not complicated and that the experimentation is routine. However, clearly, neither the specification nor the prior art provide sufficient guidance to enable the skilled artisan to make all polypeptides having chymotrypsin activity.

This rejection is respectfully traversed for the reasons of record.

The Office asserts that the claims fail to provide any structural limitation for the recited genus of variant polypeptides having chymotrypsin activity. To further prosecution, Applicants have amended claim 1 to recite in part: "the variant comprises an amino acid sequence that has at least 90% identity to amino acids 25 to 248 of SEQ ID NO: 2 of the trypsin polypeptide". Support for this amendment is found on page 4, lines 16-19, of the specification.

For the foregoing reason, Applicants submit that the new claims overcome the rejections under 35 U.S.C. § 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. The Rejection of Claims 1, 61, 130, 133, 138-140, and 143-145 under 35 U.S.C. § 112, First Paragraph

Claims 1, 61, 130, 133, 138-140, and 143-145 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Office Action stated:

> These claims are directed to a genus of variant protein molecules having chymotrypsin activity. The specification teaches the structure of only a single representative species of such proteins. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of having chymotrypsin activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that

applicants were in possession of the claimed invention.

This rejection is respectfully traversed.

The Office Action asserts that the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of having chymotrypsin activity. Applicant disagrees with this assertion. The specification on page 4, lines 16-19, provides that "the variant has chymotrypsin-like activity and has an amino acid sequence that has at least 70%, preferably at least about 75%, more preferably at least about 80%, more preferably at least about 85%, even more preferably at least about 90%, most preferably at least about 95%, and even most preferably at least about 97% identity to the amino acid sequence of the microbial trypsin". Applicants have amended claim 1 to recite in part: "the variant comprises an amino acid sequence that has at least 90% identity to amino acids 25 to 248 of SEQ ID NO: 2 of the trypsin polypeptide".

For the foregoing reasons, Applicants submit that the new claims overcome the rejections under 35 U.S.C. § 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

VII. The Rejection of Claims 1, 61, 130, 133, 138-140, and 143-145 under 35 U.S.C. § 102(b)

Claims 1, 61, 133, 138-140, and 143-145 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Hartley *et al.*, 1964, *Nature* 28: 1284-1287. The Office Action stated:

> Hartley et al. teach a chymotrypsin polypeptide having (a) substitutions at positions corresponding to positions 144, 193, 198, 201, 218, 223, 227, 228, 229, 230, and 231 of SEQ ID NO: 2, (b) deletion at positions corresponding to positions 192, 197, and 226 of SEQ ID NO: 2, and (c) an insertion between positions corresponding to positions 224 and 225 of SEQ ID NO: 2 (see enclosed alignment).

This rejection is respectfully traversed.

Under the standard required for anticipation under 35 U.S.C. § 102, the cited prior art reference is required to disclose every element of the claimed invention. *Lewmar Marine Inc. v. Barient Inc.*, 3 USPQ2d 1766 (Fed. Cir. 1987).

Hartley *et al.* disclose the amino acid sequence of bovine chymotrypsin A. Hartley *et al.* do not disclose a variant of a trypsin polypeptide, wherein the variant has chymotrypsin activity. Moreover, Example 1 provides that a comparative alignment using the Clustal method (Higgins, 1989, *CABIOS* 5: 151-153) using the LASERGENE™ MEGALIGN™ software (DNASTAR, Inc., Madison, WI) showed that the *Fusarium oxysporum* trypsin-like polypeptide engineered to the

polypeptide of SEQ ID NO: 4 having chymotrypsin-like activity shared 6.5% identity with bovine chymotrypsin A. Consequently, Hartley *et al.* do not disclose every element of the claimed invention.

For the foregoing reasons, Applicants submit that the new claims overcome the rejections under 35 U.S.C. § 102(b). Applicants respectfully request reconsideration and withdrawal of the rejection.

VIII. The Rejection of Claim 130 under 35 U.S.C. § 103(a)

Claim 130 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Hartley *et al.*, 1964, *Nature* 28: 1284-1287, in view of Hames *et al.*, 1990, Preparation and electrophoresis of polyacrylamide gels. In: Gel electrophoresis of proteins. Oxford University Press. Pp. 30-32. The Office Action stated:

> Hartley *et al.* do not teach their chymotrypsin protein in a detergent solution. Hames *et al.* teach a method for performing gel electrophoretic separation of proteins denatured by the detergent SDS (SDS-PAGE). It would have been obvious to a person *of* ordinary skill in the art to use the method of Hames *et al.* to prepare analyze the protein of Hartley *et al.* by SDS-PAGE. Motivation to do so derived from the desire to determine the purity of a recombinant preparation of the protein of Hartley et al. The expectation of success is high, as SDS-PAGE is standard in the art.

This rejection is respectfully traversed.

The Examiner has the initial burden of establishing a *prima facie* case of obviousness. A finding of obviousness under § 103 requires a determination of the scope and content of the prior art, the differences between the claimed invention and the prior art, the level of ordinary skill in the art, and whether the differences are such that the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383 US 1 (1966). Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion that the combination be made. *In re Stencel*, 828 F2d 751, 4 USPQ2d 1071 (Fed. Cir. 1987).

Hartley *et al.* is discussed in Section VII. Hames *et al.* disclose reagents for use in SDS polyacrylamide electrophoresis.

Claim 130 relates to a dertegent composition for use as a hand or laundry detergent composition (see page 39, lines 21-25, of the specification). It is well known in the art that enzymes contained in laundry detergent compositions are formulated in manner so that they are catalytically active. SDS is used in combination with urea as a denaturing agent of proteins for performing SDS polyacrylamide electrophoresis. Consequently, Hartley *et al.* in view of Hames

et al. do not teach or suggest the claimed invention. However, to further prosecution, claim 130 has been amended in part to recite "A laundry detergent composition ..."

For the foregoing reasons, Applicants submit that the new claims overcome the rejections under 35 U.S.C. § 103(a). Applicants respectfully request reconsideration and withdrawal of the rejection.

III. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: July 19, 2007

/Robert L. Starnes Reg. #41,324/
Robert L. Starnes, Ph.D.
Reg. No. 41,324
Novozymes, Inc.
1445 Drew Avenue
Davis, CA 95616
(530) 757-8100